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## WHAT IS CLAIMED IS:

- 1. An opener or activator compound which modulates the biological activity of central nervous system-associated KCNQ potassium channel polypeptides by hyperpolarizing neurons that fire before or during a migraine headache or migraine-related disorder.
- 2. An opener or activator compound which modulates the biological activity of central nervous system-associated KCNQ potassium channel polypeptides by preventing abnormal synchronous neuronal firing associated with migraine or migraine-related disorders.
- 3. The opener or activator compound according to claim 1 or claim 2, said compound selected from the group consisting of fluorooxindole and 2,4-disubstituted pyrimidine-5-carboxamide derivative compounds.
  - 4. The compound according to claim 3, wherein the opener or activator compound is (+)-3-[5-Chloro-2-[(2,2,2-trifluoroethoxy)phenyl]-1,3-dihydro-3-fluoro-6-(trifluoromethyl)-2*H*-indol-2-one or 2-(Pyrrolidin-1-yl)-4-
- 20 (trifluoromethyl)-N-[[4-(trifluoromethyl) phenyl]methyl] pyrimidine-5-carboxamide.
  - 5. The compound according to claim 1 or claim 2, wherein the KCNQ potassium channel polypeptide is selected from the group consisting of one or more of KCNQ2, KCNQ3, KCNQ4, KCNQ5, and heteromultimers thereof.
  - 6. A method of modulating neuronal activity associated with migraine or a migraine-related disorder, comprising administering to an individual in need thereof an amount of the compound according to claim 1 or claim 2 effective to inhibit neuronal activity, thereby reducing, ameliorating or alleviating migraine or a migraine-related disorder.

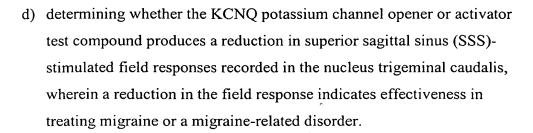
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- 7. The method according to claim 6, wherein said neuronal activity is selectively inhibited within the trigeminovascular system of the central nervous system.
- 8. A method of treating migraine or a migraine-related disorder, comprising: administering to an individual in need thereof an opener of a CNS-located KCNQ potassium channel protein, or functional portion thereof, according to claim 1 or claim 2, in an amount effective to selectively limit neuronal hyperexcitability during a migraine attack or migraine-related disorder by opening the CNS-located KCNQ potassium channel protein so as to protect against abnormal synchronous firing of neurons.
  - 9. The method according to claim 8, wherein the neuronal hyperexcitability occurs within the trigeminovascular system of the central nervous system.
  - 10. The method according to claim 6 or claim 8, wherein the KCNQ potassium channel protein is selected from the group consisting of human KCNQ2, KCNQ3, KCNQ4, KCNQ5 and heteromultimers thereof.
- 20 11. The method according to claim 6 or claim 8, wherein the CNS-located KCNQ potassium channel protein opener is a fluorooxindole compound or a 2,4-disubstituted pyrimidine-5-carboxamide derivative compound.
- 12. A method of identifying biological compounds for treating migraine or a25 migraine-related disorder, comprising:
  - a) providing a central nervous system-associated KCNQ potassium channel protein;
  - b) contacting the KCNQ potassium channel protein with a test biological compound;
- c) identifying those test compounds that are openers or activators of the
  KCNQ potassium channel protein; and

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- 13. A method of screening for candidate compounds capable of modulating activity of central nervous system-associated KCNQ potassium channel proteins and capable of treating migraine or a migraine-related disorder, comprising:
  - a) contacting a test compound with a cell or tissue expressing a KCNQ potassium channel protein;
  - b) selecting as candidate modulating compounds those test compounds that open or activate the KCNQ potassium channel protein; and
  - c) identifying those opener or activating compounds of (b) that produce a reduction in superior sagittal sinus (SSS)-stimulated field responses recorded in the nucleus trigeminal caudalis, wherein a reduction in the field response indicates effectiveness in treating migraine or a migraine-related disorder.
- 20 14. The method according to claim 12 or claim 13, optionally comprising the step of determining whether the test compound attenuates cortical spreading depression.
- 15. The method according to claim 12 or claim 13, said method comprising25 high throughput screening technology.
  - 16. The method according to claim 12 or claim 13, wherein the test compounds are small molecules, therapeutics, or drugs.